ORIGINAL ARTICLES

PSITTACOSIS AND TULAREMIA*

REPORT OF CASES—INFECTION OF TWO LABORATORY WORKERS IN CALIFORNIA: RECOVERY

I. REPORT OF CASE: PSITTACOSIS

A LABORATORY worker, who has for four years been intimately exposed to the virus of psittacosis in the form of infected birds belonging to various species, mice and human specimens (sputums and autopsy material), worked on October 6, 1935, with a heavy suspension of L. C. L. bodies (the elementary bodies regularly found in psittacosis) without wearing rubber gloves or face mask. The infective agent had been isolated and concentrated from the chorion-allantoic membrane of several developing chicks artificially inoculated with the virus. It was infective for mice in a dilution of 1.0 by 10^{-8}. On both October 12 and 13, 1935, he felt tired, and at 4:30 p. m. on October 14 he had a definite chill, when his temperature was 39.8 degrees centigrade. During the night a grippe-like general aching was accompanied by a severe pain in the lumbar region. Between 3 and 4 a. m. profuse perspiration gave relief and was followed by sound sleep. During the next four days the temperature invariably rose late in the afternoon to from 39.2 to 39.4 degrees centigrade, accompanied by sensations of chilliness, and then fell to 37 degrees after midnight, followed by perspiration. There was no headache and the night sleep of from six to eight hours was sound, free from dreams, and refreshing. The pulse varied between 76-88 and the respiration was from 10 to 20. Despite the loss of fluid during the attacks of perspiration, thirst was in no way pronounced. There was a moderate anorexia, however, and the digestion and stool were normal. A chronic bronchitis of several months' standing subsided during the first three days of the acute illness, and the absence of coughing or pharyngeal irritation was noteworthy. The nasal mucus, forcibly expelled, was slightly tinged with blood. There was no herpes labialis. On October 16, 1935, the blood examination revealed: hemoglobin, 102; red blood cells, 5,740,000; white blood cells, 5,950; granulocytes, 85 per cent; lymphocytes, 9 per cent; and mononuclears, 6 per cent. Dr. Herbert C. Moffitt examined the patient on October 16 and subsequent days, and recorded the following findings:

"Interesting points in the history were recent laboratory exposures to both psittacosis and tularemia, and a well-known immunity to all forms of Brucella infection. An associate† in the early October work had just entered the University Hospital with high temperature and indefinite pulmonary signs. There was no repetition of the initial chill, although temperature rose rapidly each afternoon for four days. Sweating was profuse for four or five nights, and was followed by rapid drop in temperature and complete relief of malaise and lumbar backache, which was severe for two days. No eruption was seen in mouth or on skin. A cough of three months ceased abruptly with onset of chill and high temperature. On October 21, for the first time tympany was noted over the right back, just inside and below the scapular angle. Cough and deep inspiration caused an explosion of fine crepitant râles, which we have learned to associate with a pneumonic process, beginning in the lower lobe near the hilus and gradually extending toward the periphery. These signs completely disappeared after three days."

Since the pulmonary signs located on October 21 were not followed by coughing, two (one gram) doses of ammonium chlorid were administered. During two coughing spells, a coffeespoonful of brownish-tinged, slightly mucoid sputum was raised on October 22, 1935. Microscopically, it showed streptococci, small and large Gram-negative rods, few Spirochaetes and fusiform organisms. A mouse test for pneumococci was negative. On the blood plates alpha streptococci, influenza and Friedlander's bacilli developed. A broth extract of the sputum inoculated intraperitoneally into mice and a ricebird gave the following results:

Mouse 19382 died on third day. Indefinite lesions.

Mouse 19383 died on seventh day. Typical gross lesions of psittacosis, with L. C. L. findings.

Mouse 19384 killed on ninth day in extremis. Typical lesions. Virus repeatedly passaged through mice and one ricebird.

Mouse 19385 killed on eleventh day. Slight lesions.

Ricebird 476 killed while ill on eleventh day. Slight lesions. Virus passaged.

A second specimen of sputum, definitely blood-tinged, collected on October 24, 1935, at a time when the daily temperature varied between 36.2 and 37 degrees centigrade, presented the same flora. The mouse test for virus was as follows:

Mouse 19390 died on tenth day. Inconclusive, due to spontaneous renal abscess.

Mouse 19391 killed on nineteenth day. Medium-sized spleen.

Mouse 19392 killed on thirty-sixth day. Large spleen, liver necrosis. Splenic suspension, when passaged, fatal to mice in five days.

Mouse 19393 killed on thirty-sixth day. Medium-sized spleen.

Despite the use of ammonium chlorid, no further sputum specimens could be procured. The blood serum collected on November 5, 1935, gave negative agglutination tests with the enteric fever antigens, B. tularense, Brucella abortus and melitensis. The complement fixation test for Brucella abortus was positive in a dilution of 0.05 (the patient is immune to the Brucella types, gives a strong allergic skin test and a phagocytic index of 30). Convalescence was decidedly slow. A general weakness foreign to the patient persisted for weeks. An x-ray film taken on November 14 showed a very faint, hazy density in the lower right lobe.

COMMENT

The observation proves again the customary saying, familiarity breeds contempt, and the general belief that continuous exposures to the virus of psittacosis may lead to a latent immunizing infection is rudely contradicted. In retrospect, it is by no means difficult to trace the disease directly to the careless handling of virus-containing material, which is in all probability far more infectious than the average bird or mice specimens. Dark-field examinations, diverse staining procedures, and the preparation of serial dilutions lend themselves to contamination of the unprotected hands. Furthermore, it is not unlikely that the virus enriched on the chick embryo may acquire new invasive properties. A German bacteriologist, who contracted psittacosis in the ten months of his intensive study of the disease, states that he contracted the infection while passaging the virus through the chicken egg.

The influenza-like character of the attack without headache would have escaped etiologic identification without the examination of the sputum. In fact, this experience lends considerable support to the belief that the mild grippe-like minor illnesses which develop in the occupational groups or households exposed to infected psittacine birds are rudimentary attacks of psittacosis. One naturally would like to know if such an attack leaves an immunity of some sort. Neutralizing antibodies, despite a severe disease, are frequently not

* Editor's Note.—The case histories here reported are those of two well-known laboratory workers in California, who were infected, respectively, with psittacosis and tularemia. Out of courtesy, names are omitted.

† See report of case of tularemia which follows as Part II of this article.

demonstrable. The complement-fixation test with the usual mouse-spleen antigen is not very dependable. Perhaps tests with purified elementary bodies may yield more definite information. Finally, one should keep in mind the possibility that the virus which exhibits such a remarkable tendency to latency may remain unrecognized in the body, but may through an intercurrent infection become mobilized. It is, doubtless, unwise to place implicit confidence in the belief that "silent," or even recognized virus infections confer a permanent protection. One must, therefore, continue to maintain appropriate precautionary measures and continuous vigilance against laboratory infections.

II. REPORT OF CASE: TULAREMIA

A case of tularemia is reported which is of interest as an infrequent type of involvement, and because of the diagnostic problem presented.

The patient, a laboratory technician in research bacteriology, was first seen on October 15, at which time she gave the following history:

Present Illness.—For the past two and one-half years she has been working with psittacosis and relapsing fever material, and for three weeks prior to onset of her illness her duties had also included the handling of material from tularemia cases. She does not recall any break in technique, pricks of hands or defective apparatus, and has always worn rubber gloves when working with infectious material. It is not unlikely that the pipetting of an uncompletely sterilized suspension of B. tularense on October 7, 1935, furnished the source of infection.

On October 10, the patient had some headache and felt unusually tired. She felt improved the following morning and went to work as usual. In the evening she felt feverish and had general aching, temperature 100.8 degrees Fahrenheit. During the night she perspired rather freely, and again felt sufficiently improved to report at the laboratory the morning of October 12. Had no appetite at noon, and left work in mid-afternoon because of extreme fatigue. Headache returned and temperature rose to 101.6 at 10 p. m. Remained in bed on Sunday, October 13, and Monday, October 14; generalized aching persisting, and with headache increasingly severe and throbbing in character. Temperature rose to a maximum of 102, and transient nausea was noted as well as suboccipital pain and slight neck stiffness.

Illness was reported on October 14, and the patient was brought into the hospital the following morning, at which time she complained of constant, severe headache, generalized, general aching, some photophobia and mental dullness. She stated there had been no chills, cough, sore throat or other respiratory symptoms. No adenopathy, no rash; bowels somewhat sluggish since onset of symptoms.

Family History and Past History.—Not significant.

Physical Examination.—Negative for cause of symptoms; no adenopathy.

Laboratory Findings.—Urine, negative; white blood cells, 7,840; polymorphonuclears, 73 per cent; agglutination positive, 1-20—typhoid and paratyphoid A and B and Brucella abortus; phagocytic index, 3.8; complement fixation Brucella, negative.

X-Ray.—Chest showed heavy root shadows, especially on right, and peribronchial infiltration extending from lower hilum on right to an area of consolidation six centimeters in diameter in upper portion of right lobe.

Physical, laboratory, and x-ray findings continued unchanged for the ensuing five days (except that no further agglutination with Brucella abortus was obtained); temperature meanwhile showing wide swings between normal and 104 degrees Fahrenheit. Subjectively continued to have troublesome headaches and slight nausea, but there were no symptoms referable to the lungs. Marked drops in temperature were associated with rather profuse diaphoresis.

October 21: The white blood corpuscle count rose to 12,750, 69 per cent polymorphonuclears; phagocytic index for Brucella, 16.36.

October 22: White blood corpuscle count was 14,350, 61 per cent polymorphonuclears. Chest examination on this date for the first time revealed moderately fine, moist râles over an area 8 to 10 centimeters in diameter on the right side posteriorly, corresponding in location to consolidation shown in x-rays of October 15 and 18, but apparently larger in extent.

October 23: Chest film showed extension of the consolidation outward and downward, with appearance of softening in the original area; blood count, 13,980; polymorphonuclears, 73 per cent.

October 24: Physical examination revealed dullness and suppressed breath sounds below the original involvement, and râles heard over a wider area than at preceding examinations.

Repeated agglutinations and blood cultures were negative during this interval, except for the above-mentioned positive agglutination in low titer, explained by past and anti-typhoid inoculation. Fever continued high; there was very slight, dry cough; and after administration of ammonium chlorid, a small amount of watery sputum, apparently mainly saliva, was obtained and injected into mice and cultured. Culture showed alpha-streptococcus, Staphylococcus aureus, m. catarrhalis, and Friedlander's bacillus.

Pulmonary involvement with slight leukocytosis, fever and headache, were suggestive of psittacosis in absence of laboratory evidence in favor of other etiology. Increasing involvement and falling white count was considered as indications of low resistance on the part of the patient, and it was deemed desirable to assume the probable etiology as psittacosis and administer convalescent serum. Twenty-five cubic centimeters of a pooled serum obtained from two recovered psittacosis patients was given on October 25, and repeated on the following day. It should be noted that one of the donors had also survived a tularemia infection.

Prompt subjective improvement was noted, and a decided drop in temperature followed the serum administration, with no subsequent rise above 100 degrees Fahrenheit.

Diagnosis was made by:

1. Agglutination test, positive, October 28 for B. tularense 1-640—4 plus, 1-1280—2 plus. November 5, for B. tularense 1-1280—4 plus.

2. Skin test October 28, which was positive October 30, with area of reaction 37 mm., central induration 8 mm.

3. Confirmed by recovery of organism B. tularense, identified by agglutination, from lesions in mice dying five to eight days following injection with sputum obtained from patient on October 25. This organism, passed into guinea-pigs, produced typical lesions of tularemia.

Progressive improvement in general condition, physical findings and x-ray evidence have been noted. Convalescence has been slow, strength returning with the reluctance characteristic of B. tularense infections. X-rays still show considerable thickening and suggest the probability of residual fibrosis, although to date each successive film has showed some improvement.

COMMENT

Of special interest is the absence of cutaneous and lymph-gland lesions and the limitation of involvement to the lungs. Presumably, infection took place by way of the respiratory tract, and the location of the lung involvement would suggest primary localization in the bronchial lymph nodes with extension from them into the lung parenchyma. Lack of positive agglutinations up to the eighteenth day, and a high phagocytic index for the Brucella organism on the eleventh day of the disease, added considerably to the problem of diagnosis.